The Prevalence of Metabolic Syndrome in Schizophrenic Patients Using Antipsychotics

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Objective: To examine the prevalence of metabolic syndrome and its risk factors in a large group of schizophrenic patients.
Methods: Sociodemographic and treatment data were collected from medical records of 1,103 inpatients and outpatients treated for schizophrenia at Seoul National Hospital in Seoul, Korea. Anthropometric measurement and blood testing were conducted for collection of physical and biochemical data and diagnosis of metabolic syndrome. Data for metabolic syndrome prevalence were compared by sex, age, metabolic syndrome markers present, treatment of markers, and types of antipsychotics and in-dividual drug agents used.
Results: Mean prevalence of metabolic syndrome in all subjects was 43.9% and 40.1% according to adapted Adult Treatment Panel III (ATP-IIIa) and International Diabetes Federation criteria, respectively. No significant differences were found in prevalence according to ATP-IIIa criteria between men (42.6%) and woman (45.9%). A trend toward higher prevalence with age was observed for both sexes until 50 years, followed by a continued increase for women but a decrease for men. Use of a combination of atypical antipsychotics was associated with the highest metabolic syndrome prevalence and use of aripiprazole with the lowest. High percentages of subjects with hypertension and dyslipidemia were not being treated for these conditions.
Conclusion: Despite their higher prevalence in schizophrenic patients, metabolic syndrome and its markers are not being ad-equately managed in these patients. Treatment of schizophrenic patients requires attention to not only their psychiatric conditions but also associated medical conditions by individual health care practitioners and hospitals as well as the public health care sector as a whole.

KEY WORDS: Antipsychotic agents; Dyslipidemias; Metabolic syndrome; Schizophrenia.

INTRODUCTION

Current treatment of patients with schizophrenia is aimed at achieving multiple goals, including control of af-fective and other types of symptoms, improved cognitive functioning, and enhanced quality of life. Schizophrenic patients typically have 20% shorter lifespans compared to the general population,[1] reflecting the high prevalence of diabetes, coronary artery disease, hypertension, and other chronic conditions in this patient population. The un-healthy lifestyle habits of many schizophrenic patients, which include poor diet, smoking, excessive alcohol con-sumption, and use of illegal substances, are believed to contribute to their higher mortality.[2]

Recent advances in pharmacology have led to the de-velopment of novel atypical antipsychotics whose use has begun a new chapter in schizophrenia treatment. Howev-er, despite their excellent therapeutic effect on positive and negative symptoms, including affective symptoms, and cognitive functions, some atypical antipsychotics have various side effects, including weight gain, develop-ment of diabetes, abnormal changes in serum lipid levels, negative effects on the heart, increase in serum prolactin levels, development of cataracts, and sexual dysfunc-tion.[2]

When it was first identified, metabolic syndrome (MS) was referred to as insulin resistance syndrome because many patients identified with the disorder were elderly pa-tients with coronary artery disease, among whom insulin resistance is a common characteristic.[3] In 1998, the World Health Organization (WHO) renamed the disorder MS and developed the first set of diagnostic standards.[4] Since then, the standards for diagnosis of MS have changed many times. Currently, researchers and clinicians in South

Korea use one or both of two sets of criteria, either the adapted Adult Treatment Panel III (ATP-IIIa) criteria,[5] which were developed by the National Cholesterol Education Program (NCEP), and/or the International Diabetes Federation (IDF)[6] criteria for diagnosis of MS. Regarding diagnosis of central obesity, one of the criteria for diagnosis of MS, South Korean researchers and clinicians use the WHO-recommended standards for central obesity in Asians, as Asians have different body measurements compared to Caucasians.[7] According to the ATP-IIIa, a set of diagnostic criteria, diagnosis of MS is warranted if 3 of the following 5 markers are present: central obesity, abnormal triglyceride (TG) level, abnormal high-density lipoprotein (HDL) cholesterol level, abnormal blood pressure, and/or abnormal blood glucose level. According to the IDF criteria, central obesity is an essential factor in MS, and thus MS should be diagnosed if central obesity and 2 of the other 4 markers are present.

According to one epidemiological study, schizophrenic patients are at high risk of MS and experience diabetes and obesity at twice the rate that the general population does.[8] This finding was supported by the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study of 1,460 schizophrenic patients, which found the prevalence of MS using the ATP-IIIa to be 36.0% in the male patients and 51.6% in the female patients examined.[9] While the characteristics of MS may vary, depending on ethnicity and socioeconomic status, lack of physical activity, isolation, high alcohol consumption, smoking, poor diet, and use of medical substances all contribute to higher prevalence of MS in schizophrenic patients in all populations. An important consideration in comparison of MS prevalence among populations is the need for adjustment for differences in Asian body measurements, which results in higher MS prevalence in Asian populations.[10]

The effects of atypical antipsychotics on the metabolic markers included in the diagnostic criteria for MS have been extensively researched. When obesity is defined as a body mass index (BMI) of or greater than 27 kg/m^2, 42% of schizophrenic patients are considered obese as compared to 27% of the general population,[11] reflecting the knowledge that use of atypical antipsychotics causes weight gain.[12-14] For these reasons, schizophrenic patients on antipsychotics are advised to regularly measure their weight and waste circumference.[2] Schizophrenic patients are also more likely to develop type 2 diabetes mellitus, with which certain types of atypical antipsychotics have been associated, compared to the general population.[15-17]

In consideration of these findings, as well as reports that

several atypical antipsychotics may significantly raise blood glucose,[18] schizophrenic patients are advised to undergo regular monitoring for diabetes.[2] Among the American Diabetes Association (ADA) risk factors for diabetes, which include BMI $\geq$25 kg/m^2, family history of diabetes, habitual inactivity, ethnicity, hypertension, HDL cholesterol $\leq$35 mg/dl, TG $\geq$250 mg/dl, and abnormal blood glucose levels,[19] abnormal lipid levels have been associated with use of several atypical antipsychotics.[17] To further investigate previous findings regarding the association between schizophrenia and MS, specifically the higher prevalence of MS markers in schizophrenic patients than in the general population and the association between use of atypical antipsychotics and development of MS, this study evaluated the prevalence of MS according to ATP-IIIa and IDF criteria in South Korean schizophrenic patients who had been using atypical antipsychotics for at least 1 year prior to initiation of the investigation.

METHODS

Subjects

This study enrolled both inpatients and outpatients being treated at Seoul National Hospital from October 2007 to May 2011. Subjects were schizophrenic patients diagnosed by Diagnostic and Statistical Manual Text Revision (DSM-IV-TR) diagnostic criteria[20] and were currently taking antipsychotic medication. Inclusion criteria were age 18-65 years continuous use of antipsychotic agents for at least 1 year prior and up to study initiation, and the ability to provide informed consent. Exclusion criteria were pregnancy, female patients currently taking contraceptives, and female patients on hormone therapy for various reasons. Outpatients, visiting on certain dates were randomly selected and the study's purpose and method were explained to them. Inpatients hospitalized for a certain period were selected in using the same selection procedure mentioned above Use of the selection procedure resulted in the enrollment of 1,103 patients (317 inpatients and 786 outpatients). This study was authorized by the institutional review board of Seoul National Hospital.

Sociodemographic Characteristics and Clinical Parameters

After the patients had provided voluntary consent, blood samples were drawn for measurement of biochemical parameters and medical records reviewed for collection of sociodemographic data. Patient records were

reviewed and interviews conducted to collect data regarding patient age; demographic characteristics; family history; disease duration; level of education; use of nicotine and/or alcohol; Clinical Global Impression-Severity (CGI-S) score; type and dose of currently administered antipsychotics; use of concomitant medication; and diagnosis and treatment of diabetes, hypertension, and/or dyslipidemia. To facilitate investigation of the association between MS and each of the 12 types of antipsychotics currently administered, the types of antipsychotic agents taken by patients were divided into the following groups to assess their effects in each sex: a first-generation agent (FGA) or typical antipsychotic group; a second-generation agent (SGA) or atypical antipsychotic group; an FGA combination group; and FGA and SGA combination group; and an SGA combination group. The subjects were also divided into 5 age groups (20-29 years, 30-39 years, 40-49 years, 50-59 years, and 60 years and above) to assess the prevalence of MS in each group by sex. The subjects were also divided into groups according to the presence of each MS marker to evaluate its prevalence in each sex.

To evaluate adherence to treatment guidelines, the treatment rate for each MS marker was evaluated. Diabetes was defined as a fasting blood glucose (FBG) level of ≥ 126 mg/dl or current treatment for diabetes; hypertension as a systolic blood pressure of ≥ 140 mmHg, a diastolic blood pressure of ≥ 90 mmHg, or current treatment; dyslipidemia as an HDL cholesterol level of < 40 mg/dl in men and < 50 mg/dl in women or TG level of ≥ 150 mg/dl, or current treatment.

Anthropometric Measurement and Blood Testing

The height, weight, and BMI of all subjects were measured at the Clinical Research Center of Seoul National Hospital. Height and weight of inpatients were measured while wearing a patient uniform and of outpatients after removal of coat and shoes. Blood pressure was measured while in a sitting position after a 10-minute rest and waste circumference was measured by application of a tape measure between the iliac crest and lower rib while in a standing position. The same tools were used for measurement of all patients. Venous blood was collected in the morning after an overnight fast of at least 12 hours for determination of MS markers, including FBG, HDL, and TG level, as well as total cholesterol level, a marker of dyslipidemia.

MS Diagnostic Criteria

MS was diagnosed according to the ATP-IIIa[5] and IDF criteria[6] and central obesity identified using the WHO criterion for central obesity in Asian populations.[7] Whereas the ATP-III criterion for central obesity is waist circumference of ≥ 102 cm in men and ≥ 88 cm in women for Caucasians, it is ≥ 90 cm in men and ≥ 80 cm in women for Asians. Diagnosis of MS was based on evaluation of the 5 established markers of the disease: (1) central obesity, defined as a waste circumference of ≥ 90 cm in men and ≥ 80 cm in women; (2) hypertension, defined as a systolic value of ≥ 130 mmHg, a diastolic value of ≥ 85 mmHg, or being under treatment for hypertension; (3) abnormal FBG level, defined as ≥ 10 mg/dl or diagnosis with type 2 diabetes mellitus; (4) abnormal HDL cholesterol level, defined as < 40 mg/dl in men and < 50 mg/dl in women or currently undergoing treatment; and (5) abnormal TG level, defined as ≥ 150 mg/dl or currently undergoing treatment. The ATP-IIIa specifies diagnosis of MS when central obesity, considered the essential marker, is present with at least 3 of the remaining 4 markers, whereas the IDF specifies diagnosis when central obesity is present with at least 2 of the remaining 4 markers.

Statistical Analysis

Continuous variables in the comparison of subject's basic characteristics were expressed as means and standard deviations. Group comparison was performed using the t test, differences in frequency of the nature of criteria used were analyzed using the Kruskal-Wallis chi-square (χ^2) test, a non-parametric method.

For comparison of overall prevalence of MS according to sex, comparison of prevalence in age groups according to sex, comparison of presence of the five diagnostic markers of MS according to sex, comparison of types of drugs currently used, comparison of prevalence per drug type, and comparison of prevalence according to BMI, the chi-square test was used.

SPSS software 12.0 version (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses and statistical significance was determined as p value < 0.05.

RESULTS

Sociodemographic and Anthropometric Characteristics

Comparison of the mean age of the 674 men (40.5±9.6 years) and 429 women (43.1±9.7 years) enrolled in this study of 1,103 subjects indicated that the women were significantly older than the men ($p < 0.001$). Comparison of

the years of education obtained indicated that the men (12.1±2.6 years) had attained a significantly higher level of education than the women (11.5±3.1 years) ($p < 0.001$). Comparison of the mean disease duration of the men (17.7±8.3 years) and women (18.5±8.5 years) indicated that there was no significant difference. The mean CGI-S score for the men (3.7±0.8) and women (3.6±0.9) did not differ significantly. Comparison of prevalence of family history of diabetes, hypertension, and/or dyslipidemia in 306 men (45.4%) and 193 women (45.0%) indicated that there was no significant difference. Comparison of prevalence of smoking, which was 44.7% in all subjects, in 419 men (62.1%) and 75 women (17.5%) indicated that it was significantly higher in men (x^2=211.05, $p < 0.001$). Concomitant use of antipsychotics with other drugs was 80.5% of all subjects, in 551 men (81.8%) and 337 women (78.6%) indicated that there was no significant difference (Table 1).

The mean height of the male and female subjects was 170.6±6.5 cm and 157.1±9.6 cm, respectively; the mean weight 73.3±13.2 kg and 64.9±13.9 kg, respectively; the mean BMI 25.1±4.2 kg/m^2 and 26.0±4.8 kg/m^2, respectively; the mean FBG level 91.8±23.4 mg/dl and 94.7±30.4 mg/dl, respectively; the mean HDL cholesterol level 42.7±10.0 mg/dl and 49.7±13.9 mg/dl, respectively;

the mean TG level 174.4±117.5 mg/dl and 141.0±93.6 mg/dl, respectively; the mean total cholesterol 188.0±41.3 mg/dl and 196.0±42.4 mg/dl, respectively; the mean systolic blood pressure 122.7±14.4 mmHg and 118.6±15.2 mmHg, respectively; and the mean systolic blood pressure 79.8±10.9 mmHg and 77.8±11.2 mmHg, respectively.

Among all subjects, 116 (10.5%) were found to have diabetes, 277 (25.1%) hypertension, and 673 (61.0%) dyslipidemia. Regarding treatment of these conditions at the time of the study, 80 of the 116 (69.0%) patients found to have diabetes were being treated for the condition, 83 of the 277 (30.0%) found to have hypertension were being treated, and only 31 of the 673 (4.6%) found to have dyslipidemia were being treated (Table 2).

Prevalence of MS

The prevalence of MS in all subjects was 43.9% according to ATP-IIIa criteria and 40.1% according to IDF criteria. Comparison of MS prevalence in male and female subjects according to ATP-IIIa criteria, which was 42.6% in men and 45.9% in women, indicated no significance difference in prevalence by sex (x^2=1.187, p=0.152). However, comparison according to IDF criteria, which was 37.7% in men and 43.8% in women, indicated a significantly higher prevalence in women (x^2=4.112, p= 0.025) (Table 3).

Comparison of prevalence of MS by age group according to ATP-IIIa criteria, which was 29.8% between age 20 and 29 years, 42.5% between age 30 and 39, 45.5% be-

Table 1. Subject sociodemographic data (N=1,103)

Variable	Male	Female	p value
All subjects	674	429	
Outpatients	456 (67.7)	330 (76.9)	
Inpatients	218 (32.3)	99 (23.1)	
Age (year)	40.5±9.6	43.1±9.7	<0.001
Education (year)	12.1±2.6	11.5±3.1	<0.001
Duration of illness (year)	17.7±8.3	18.5±8.5	0.116
CGI-S score	3.7±0.8	3.6±0.9	0.345
Smoker	419 (62.1)	75 (17.5)	<0.001
Taking medication concurrently			0.110
Yes	551 (81.8)	337 (78.6)	
No	123 (18.2)	92 (21.4)	
Family history of medical illness			0.786
Yes	306 (45.4)	193 (45.0)	
No	355 (52.7)	230 (53.6)	
Unknown	13 (1.9)	6 (1.7)	
Types of antipsychotic agents			0.051
Typical (TA)	61 (9.1)	47 (11.0)	
Atypical (AAP)	365 (54.1)	242 (56.4)	
TA+TA combination	25 (3.7)	9 (2.1)	
TA+AAP combination	103 (15.3)	56 (13.0)	
AAP+AAP combination	115 (17.1)	72 (16.8)	
More than triple agents	5 (0.7)	3 (0.7)	

Values are presented as number only, number (%), or mean± standard deviation.
Medical illnesses assessed were diabetes mellitus and hypertension; CGI-S, Clinical Global Impression-Severity.

Table 2. Prevalence of diagnosis and treatment of diabetes mellitus, hypertension, and dyslipidemia in study subjects (N=1,103)

Disease	Diagnosed	Treated	Untreated
Diabetes mellitus	116 (10.5)	80 (69.0)	36 (31.0)
Hypertension	277 (25.1)	83 (30.0)	194 (70.4)
Dyslipidemia	673 (61.0)	31 (4.6)	642 (95.4)

Values are presented as number (%).
Diabetes mellitus was defined as fasting blood sugar level ≥126 mg/dl or current ongoing treatment; hypertension as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or current ongoing treatment; and dyslipidemia as high-density lipoprotein level of <40 mg/dl in males and <50 mg/dl in females, triglyceride level of ≥150 mg/dl, or current ongoing treatment.

Table 3. Prevalence of metabolic syndrome in study subjects

Diagnostic criteria	All (%, N=1,103)	Male (%, n=674)	Female (%, n=429)	x^2	p value
ATP-IIIa	43.9	42.6	45.9	1.187	0.152
IDF	40.1	37.7	43.8	4.112	0.025

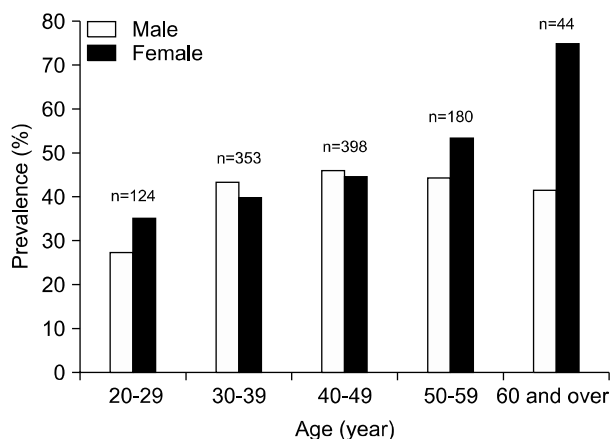ATP-IIIa, adapted Adult Treatment Panel III; IDF, International Diabetes Federation.

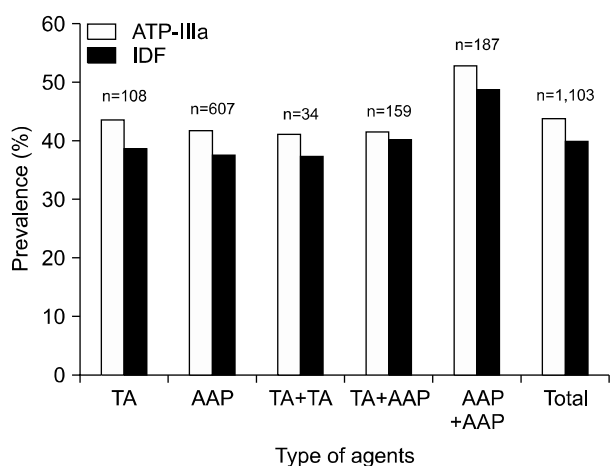**Fig. 1.** Prevalence of metabolic syndrome by age group.

Fig. 2. Prevalence of metabolic syndrome by types of agents. ATP-IIIa, Adult Treatment Panel III; IDF, International Diabetes Federation; TA, typical agent; AAP, atypical agent.
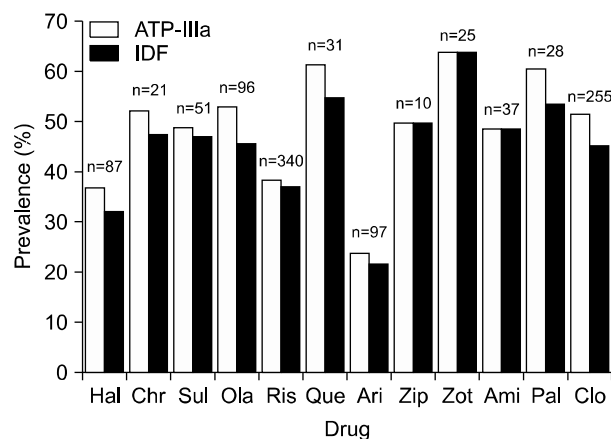

Fig. 3. Prevalence of metabolic syndrome by individual agent. ATP-IIIa, Adult Treatment Panel III; IDF, International Diabetes Federation; Hal, haloperidol; Chr, chlorpromazine; Sul, sulpiride; Ola, olanzapine; Ris, risperidone; Que, quetiapine; Ari, aripiprazole; Zip, ziprasidone; Zot, zotepine; Ami, amisulpride; Pal, paliperidone; Clo, clozapine.

tween age 40 and 49, 48.9% between age 50 and 59, and 56.8% age 60 and over, indicated a steady increase in prevalence with age (χ^2=15.444, p=0.004). On the other hand, comparison of MS prevalence by sex revealed that prevalence in men increased from 27.4% between the ages 20 and 29 years to 46.1% between the age of 40 and 49, then decreased to 44.4% between the age of 50 and 59 years and 41.7% at the age of 60 years and over. In contrast, MS prevalence in women steadily increased from 35.0% between the age of 20 and 29 years to 75.0% at the age of 60 years and over (χ^2=12.398, p=0.015). Comparison of MS prevalence in subjects aged 60 years and over indicated a significantly higher prevalence in women in this age group (χ^2=4.940, p=0.027) (Fig. 1).

The prevalence of MS according to ATP-IIIa criteria by type of agent was found to be 44.4% in the FGA group,

41.7% in the SGA group, 41.2% in the FGA combination group, 41.5% in the FGA and SGA combination group, and 52.9% in the SGA combination group. Although no significant differences were found among the groups regarding MS prevalence (χ^2=7.906, p=0.095), the SGA combination group was found to have the highest MS prevalence, which was overall and 49.6% in men and 58.3% in women. Comparison of MS prevalence according to type of agent by sex indicated no significant differences in prevalence (men: χ^2=3.896, p=0.420; women: χ^2=8.916, p=0.063) (Fig. 2).

MS prevalence according to ATP-IIIa criteria for each of the 12 drugs examined were as follows: haloperidol, 36.8% (n=87); chlorpromazine, 52.4% (n=21); sulpiride, 49.0% (n=51); olanzapine, 53.1% (n=96); risperidone, 38.5% (n=340); quetiapine, 61.3% (n=31); aripiprazole, 23.7% (n=97); ziprasidone, 50.0% (n=10); zotepine, 64.0% (n=25); amisulpride, 48.6% (n=37); paliperidone, 60.7% (n=28); and clozapine, 51.4% (n=255). According to the type of drug used, there was a difference in the prevalence of MS (χ^2=54.440, $p<0.001$) (Fig. 3).

Prevalence of MS Markers

Comparison of the prevalence of MS markers in the male and female subjects revealed a significantly higher prevalence of hypertension (42.6% vs. 35.9%, respectively; χ^2=4.881, p=0.016) and abnormal TG level (49.3% vs. 35.9%, respectively; χ^2=18.986, $p<0.001$), but a significantly lower prevalence of central obesity (56.4% vs. 77.6%, respectively; χ^2=51.755, $p<0.001$)

Table 4. Prevalence of metabolic syndrome markers (N=1,103)

Parameter	All (%)	Male (%)	Female (%)	χ^2	p value
Abdominal obesity (waist circumference ≥90 cm in males and ≥80 cm in females)	64.6	56.4	77.6	51.755	<0.001
Elevated fasting blood sugar (≥100 mg/dl or current ongoing treatment)	24.6	24.0	25.4	0.266	0.328
Elevated blood pressure (systolic ≥130 mmHg, diastolic ≥85 mmHg, or current ongoing treatment)	40.0	42.6	35.9	4.881	0.016
Low high-density lipoprotein cholesterol level (<40 mg/dl in males and <50 mg/dl in females or current ongoing treatment)	48.4	43.5	56.2	16.944	<0.001
Elevated triglyceride level (≥150 mg/dl or current ongoing treatment)	44.1	49.3	35.9	18.986	<0.001

and low HDL cholesterol level (43.5% vs. 56.2%, respectively; χ^2=16.944, $p < 0.001$) in the male subjects. Comparison of prevalence of impaired FBG, which was found in 24.0% of men and 25.4% of women, revealed no significant differences between the sexes (χ^2=0.266, p=0.328) (Table 4).

Comparison of MS prevalence according to BMI, which among all subjects was ≤19.9 kg/m^2 for 8.6%, 20.0-24.9 kg/m^2 for 25.3%, 25.0-29.9 kg/m^2 for 59.5%, and ≥30 kg/m^2 for 76.7%, indicated significant differences in MS prevalence according to degree of obesity (χ^2=223.381, $p < 0.001$). Comparison of MS prevalence according to degree of obesity by sex also revealed significant differences (men: χ^2=126.763, $p < 0.001$; women: χ^2=95.996, $p < 0.001$).

DISCUSSION

Among previous studies that investigated the relationship between markers of MS and other diseases, Kim et al.[21] identified abnormally high central obesity and abnormal TG level, hypertension, and abnormal FBG level as risk factors for coronary artery disease, regardless of age and sex. Among those that investigated the relationship between MS and conditions associated with it, Isomaa et al.[22] identified a 3-fold increase in risk of congestive heart failure and stroke in patients with MS compared to those without MS. Consideration of such findings indicates that regular screening of schizophrenic patients for MS should be integrated into current treatment guidelines. To provide support for the findings of previous studies and their implications, this study examined a large group (n=1,103) of schizophrenic patients to examine the prevalence of MS and the risk factors for MS and compare the prevalence by patient and treatment variables. Using ATP-IIIa criteria, the prevalence of MS in the schizophrenic patients examined in this study was found to be 43.9%, a prevalence markedly higher than the 31.3% reported by the Korean National Health and Nutrition

Examination Survey,[23] a 2007 study of 2,890 healthy Korean adults over the age of 20 conducted by the Ministry of Health and Welfare that also used ATP-IIIa criteria. The prevalence in the female subjects was found to be 45.9%, which, although slightly higher than the 42.6% prevalence found in the male subjects, was not significantly higher than the prevalence found in the male subjects. On the other hand, using the IDF diagnostic criteria, 43.8% of the female subjects were found to have MS, a prevalence significantly higher than the 37.7% prevalence found in the male subjects. This finding accords with the Korean National Health and Nutrition Examination Survey finding of an MS prevalence of 32.9% in women, a prevalence significantly higher than the 29.0% prevalence found in men.

Regarding MS prevalence according to age group by sex, female subjects age 60 and over were found significantly more likely to have MS than male subjects in the same age group. Although the differences between the sexes did not reach a level of statistical significance for any other age groups, analysis of the data revealed a trend toward higher prevalence between the age of 20 and 29 years and between 50 and 59 years, but a lower prevalence between 30 and 39 years and between 40 and 49 years, in female subjects compared to male subjects. Regarding MS markers, significantly higher prevalence of hypertension and elevated TG level but significantly lower prevalence of central obesity, elevated FBG level, and low HDL cholesterol level were found in the male subjects compared to the female subjects.

Using WHO criteria for overweight and obesity of a BMI of 25-29.9 kg/m^2 and a BMI of 30 kg/m^2 and over, respectively, 49.6% of the male subjects and 55.2% of the female subjects were found to be overweight and 10.5% the male subjects and 20.5% the female subjects to be obese. Among these subjects, 59.5% of overweight and 76.7% of obese patients were found to have MS. Regarding central obesity, 56.4% of the male subjects and 77.6% of the female subjects were found to be centrally obese,

figures much higher than the 27.5% and 51.2%, respectively, reported in the 2007 Korean National Health and Nutrition Examination Survey. This finding accords with the previous findings that 8 of 10 female schizophrenic patients are centrally obese and that male schizophrenic patients, although having a lower prevalence of central obesity compared to female patients, have a 2-fold higher prevalence of obesity compared to the general population. As schizophrenic patients appear to be more obese compared to the general population due to the wide availability of high-calorie foods and inactivity, it is deemed necessary to regularly monitor central obesity and other risk factors for obesity prevention, treatment, and management. Obese individuals face increased risk of diabetes, cardiovascular disease, hypertension, and certain types of cancer as well as a 50% to 100% higher risk of premature death compared to normal weight indivduals.[24] Moreover, as visceral obesity increases production of free fatty acids from adipocytes and directly increases insulin resistance, its excessive accumulation increases risk of MS.[25]

These findings strongly suggest that weight-management guidelines should be included in the treatment of schizophrenic patients.

Although analysis of the data indicated that prevalence of MS increased with age, age-related trends in MS prevalence appear to differ by sex. For the male subjects, MS prevalence was found to be 27.4% between the age of 20 and 29 years, 43.6% between 30 and 39 years, 46.1% between 40 and 49 years, 44.4% between 50 and 59 years, and 41.7% aged 60 years and above, revealing an increase in prevalence until between the ages of 40 and 49 years followed by a decrease at the age of 50 years. In contrast, the prevalence in female subjects was found to steadily increase with age. Considering the fact that both male and female schizophrenic patients have a 20% shorter longevity compared to the general population[1] but that all women, although generally found to have a longer mean lifespan compared to men, experience age-related physical and hormonal changes that may negatively impact MS markers,[23] premature death from various conditions, including cardiovascular disorders, may explain the drop in prevalence in men but not in women beginning at age 50.

The CATIE study[26] found that diabetes in 10.4%, hypertension in 33.2%, dyslipidemia in 63.3% of the schizophrenic patients that it examined and 30.2% with diabetes, 62.4% with hypertension, 88.0% with dyslipidemia were not being treated at the time that the study was conducted.

In contrast, diabetes was found in 10.5%, hypertension in 25.1%, and dyslipidemia in 61.0% of the subjects examined in the present study. The percentage of subjects in the present study currently being treated for these conditions was found to be 69.0% for diabetes, 30.0% for hypertension, and 4.6% for dyslipidemia. The higher treatment rate for diabetes may reflect the fact that diabetes is more widely recognized in society, leading to higher likelihood of diagnosis and treatment. Nevertheless, diagnosis and treatment of hypertension and, especially, dyslipidemia is also important, and its importance should be more widely recognized.

Schizophrenic patients tend to have predisposing factors, such as indifference to their condition, habitual inactivity, high prevalence of smoking, and malnutrition, as well as the experience of a mental condition itself and its symptoms, that make them susceptible to medical diseases. They are also likely to be underdiagnosed and undertreated. The 2007 Korean National Health and Nutrition Examination Survey revealed a trend toward lower prevalence of hypertension and higher rate of treatment of hypertension in the general Korean population due to a decreasing number of smokers and greater social awareness of the importance of consuming a low-sodium diet. The prevalence of smoking in the study subjects was found to be 62.1% in men, which is markedly higher than that of the general population. Considering the negative impact of smoking on the development of various severe diseases, educational and treatment programs should be implemented to reduce the high prevalence of smoking among schizophrenic patients. Moreover, the relatively low percentage of study subjects being treated for chronic conditions, especially dyslipidemia, for which only 4.6% of the study subjects who had the condition were being treated, calls for more active intervention in terms of diagnosis and treatment.

These findings reflect the fact that despite growing recognition of the importance of diagnosis and treatment of diabetes and hypertension, the general population does not view dyslipidemia as a condition requiring treatment, leading treatment efforts to lag behind those of other conditions. The findings of previous studies, including identification of an association between MS and cardiovascular disease,[21] lack of treatment of MS risk factors in a high percentage of schizophrenic patients, and degradation of medical service quality for these patients, may all be related to the higher mortality of schizophrenic patients compared to the general population.[27] In this light, expanding public healthcare services for schizophrenic

patients takes on greater importance.

No significant differences were found regarding MS prevalence between men and women, nor among patients who used different types of medications. However, the MS prevalence of the SGA combination group was found to be 52.9%, which is higher but not significantly so than the MS prevalence of 44.4% in the FGA group, 41.7% in the SGA group, 41.2% in the FGA combination group, and 41.5% in the FGA and SGA combination group. This finding, as well as that of an even higher MS prevalence of 58.3% in the female subjects in the SGA combination group, accords with previous research indicating that drug treatment consisting of a combination of antipsychotics, in particular atypical antipsychotics, may increase the risk of MS.[28,29] Considering that no significant differences were found regarding disease duration according to the type of agent, schizophrenic patients taking a combination of SGAs appear to have a lower prevalence than those taking a combination of FGAs, but the differences in prevalence found according to type of agent may lead to erroneous interpretation of the results. Comparison of prevalence by individual agent revealed an MS prevalence of 36.8% (n=87) in subjects taking haloperidol, one of the most widely used antipsychotics, which was lower than the overall study mean of 43.9%. In contrast, the prevalence of MS was higher than the mean in subjects taking atypical antipsychotics except for those taking aripiprazole 23.7% (n=97) or risperidone 38.5% (n=340). The study subject taking aripiprazole, an atypical antipsychotic with partial agonist action that has been reported to have low impact on weight gain, blood glucose, and lipid metabolism,[30,31] were not found to significantly differ from the other subjects in terms of mean duration of disease and mean period of medication. However, the results indicate that use of combination therapy may impact MS markers, such as weight gain, which was experienced 62.9% of subjects undergoing combination therapy compared to the overall mean of 80.5%. When other variables that may impact the diagnosis of MS, such as physical characteristics, diet, activity level, and socioeconomic status, are considered, the low prevalence of 23.7% in subjects taking aripiprazole cannot be solely explained by type of medication used. Nevertheless, analysis of the data collected from a large sample (n=97) of patients supports previous findings that aripiprazole has a low negative impact on MS markers.

This study faced several limitations that may affect the generalizability of the results. First, as the study subjects were patients at a single mental hospital, the results obtained from their examination cannot be generalized to the entire population of schizophrenic patients in Korea. Second, variables that can impact MS, such as physical condition, diet, severity of symptoms, physical activity level, and socioeconomic status, were unable to be adequately evaluated. Third, although it was assumed that blood collection had been conducted after a 12-hour fast, the exact duration of the fast could not be determined for several patients. Despite these limitations, this study was able to make major contributions to the literature by its examination of a large sample of schizophrenic patients to evaluate not only the prevalence of MS and MS markers among them but also the nationwide problem of lack of proper treatment for medical conditions other than psychiatric problems in this patient population.

This study yielded several notable findings that should be considered in the future research and treatment of schizophrenic patients. First, the prevalence of MS in the study subjects was found to be significantly higher than that of the general population, calling for more efforts in MS diagnosis and treatment in schizophrenic patients. Second, the severity of obesity, including central obesity, was higher in the study subjects compared to the general population, indicating that therapeutic interventions, including weight management and dietary improvement, are needed for schizophrenic patients. Third, a remarkably low percentage of the study subjects were being treated for hypertension and, especially, dyslipidemia compared to diabetes, calling for greater emphasis on diagnosis and treatment of these conditions. In conclusion, treatment of schizophrenic patients requires attention to not only their psychiatric conditions but also associated medical conditions by individual health care practitioners and hospital as well as the public health care sector as a whole.

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